# EXHIBIT 25

# DEFEAT CHRONIC PAIN NOW!

GROUNDBREAKING STRATEGIES FOR ELIMINATING THE PAIN OF ARTHRITIS, BACK AND NECK CONDITIONS, MIGRAINES, DIABETIC NEUROPATHY, AND CHRONIC ILLNESS

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A Portion of Author Proceeds Will Be Donated to the Reflex Sympathetic Dystrophy Syndrome Association and the American Pain Foundation

## Although each pain condition may have particular medications that in general responds better than others, the same rules apply for picking first-line versus second-line and third-line drugs.

Try the ones with proven efficacy (i.e., pain-relieving abilities demonstrated in studies that compare the medication versus placebos) and with the least amount of potential side effects. Thus, just as the FDA evaluates drugs, you should always weigh a drug's benefits and risks for a so-called benefit:risk ratio, i.e., you need to find out if the chances are greater you will obtain more pain relief than side effect. Medications-for-pain can be divided into these categories:

- ✓ "Painkillers": anti-inflammatory drugs, nonsteroidal anti-inflammatory drugs (NSAIDs), cox-2 specific drugs, and acetaminophen
- ✓ Topical medicines
- ✓ Antiseizure medications
- ✓ Antidepressants
- ✓ Opioids (sometimes referred to as *narcotics*—because the term *narcotic* actually includes non-opioid medications that do not treat pain, we do not feel it is appropriate to use the term when describing an opioid drug)

## The Golden Rule for Medication for Pain

A successful medication should reduce your pain with limited side effects, resulting in your ability to be more active. Put simply:

- If the good (pain relief) outweighs the bad (side effects) and you are noticing an improvement in your ability to participate in your normal daily activities, your current medication is a good fit for you.
- If the bad outweighs the good and you are not noticing a meaningful reduction in your pain at the highest tolerated dose, or if you are having bad side effects, your medication is not appropriate for you and should be discontinued (under supervision by your doctor).

## Rules For Taking Medications, Part I

When taking medications for pain, there are a few simple rules to follow. Keeping these in mind will help you become a co-director in managing your medication regimen.

### RULE 1: EVERY PERSON IN PAIN IS DIFFERENT

Just because your friend with the same pain condition gets good pain relief from a certain drug doesn't mean you will too. And even if the two of you experience relief from the same medication, the doses that deliver that relief may be very different. Also, one of you may experience side effects from a certain drug and the other may not.

### RULE 2: ALWAYS CHANGE DOSES ONE DRUG AT A TIME

Your doctor should always start every medicine at the lowest possibly effective dose and gradually increase it by the lowest possible increment every three to seven days (depending on the medicine and how you are reacting to it with regard to the amount of pain relief and side effects you experience). Remember, your doctor should do this with only one drug at a time.

### RULE 3: KEEP IN CLOSE CONTACT WITH YOUR DOCTOR WHEN ADJUSTING YOUR DOSES

When your doctor changes your medication, you should contact your doctor or his staff at least once per week until the dose is stable. If you ever have any questions, you should immediately call the doctor's office for answers.

### RULE 4: YOU MUST BE AN ACTIVE PARTICIPANT IN YOUR TREATMENT

Trying to find the best pain relief with medicines (or any other treatments) requires that you take some responsibility. You must tell your doctor what changes have occurred with the medicine, good and bad, and follow his or her advice closely. If you have started a new medication for any medical condition—even an antibiotic for an infection—you should inform your doctor of this change because it may actually interfere with the pain treatment that your doctor has prescribed for you. By reading this book, you are learning how to best do this and are becoming your most important advocate!

### WHAT IS "OFF-LABEL USE" OF PAIN MEDICATIONS?

Many, if not most, of the medications doctors (especially pain doctors) prescribe to their patients are off label, meaning the medication is being prescribed to treat a condition that has not been FDA-approved for that condition. You should realize that this practice is very common, and usually is based on your doctor's experience with the drug in similar patients and on his or her reading of studies in the medical journals showing good results with the drug for your condition.

Often, a drug company will not pursue FDA approval for a pain condition because either it is too costly or the drug's patent life will expire before the FDA will approve the new indication, and thus a generic copycat will be available before the company can obtain a return on its investment (the investment to obtain FDA approval for a drug is often more than tens of millions, even hundreds of millions of dollars). But your doctor should inform you when he or she is prescribing a medication off label and why he or she thinks it will help you. This is an absolutely allowed practice in the United States.

## Frequently Asked Questions For Managing Pain

It is only natural to feel confused by the many facets of pain management—even for doctors, this is complicated stuff! In this section, we outline some of the most frequently asked questions on the topic of medication for pain.

### WHAT MAKES A SUCCESSFUL MEDICATION FOR PAIN?

It is critical to have realistic expectations. Unfortunately, with one medication, most people with chronic pain do not experience a reduction in pain of greater than 50 percent, although it may be possible to experience near complete pain relief with the right mixture of medications at the right dose working with appropriate nonmedication treatments. Still, it is important to accept that, even with the best treatment, you will likely not achieve 100 percent relief from your chronic pain. "Success" in pain management is measured not only by the degree of pain relief, but also by achieving this relief without intolerable side effects, while increasing your ability to function and participate in desired activities.

### Alert! Over the Counter (OTC) Doesn't Guarantee Safety

Just because a drug is available OTC without a prescription does not mean it is safe or has proven pain-relieving capabilities. Acetaminophen (Tylenol) has very serious potential side effects, such as liver toxicity, and oral NSAIDs (Motrin, Advil, ibuprofen, aspirin, Aleve, naproxen) can all cause very serious kidney abnormalities if not taken in proper doses. Also, most of the OTC pain creams/gels/patches (Bengay, Icy Hot) have little to no proven efficacy.

### Names of NSAID Medications (Brand Names)

- Ibuprofen (Advil, Motrin)
- Naproxen (Aleve)
- Ketorolac (Toradol)
- Diclofenac (Voltaren, Pennsaid)
- Acetaminophen (Tylenol*) (In countries other than the United States, it is called Paracetamol.)

* Acetaminophen is not technically an NSAID, but for our purposes we'll put it here. Acetaminophen, like the NSAIDs, does inhibit cyclooxygenase (COX), an enzyme responsible for the production of prostaglandins, which are important mediators of inflammation and pain. However, acetaminophen has little true anti-inflammatory action and believe it or not, its true pain-relieving mechanism is still not known.

## WHEN SHOULD YOU STOP TAKING A MEDICATION FOR PAIN?

You should stop taking a medication for pain if either of the following occurs:

- If after you achieve the highest-tolerated dose of a medication, the medication does not reduce your pain in a meaningful way, you should stop taking that medication. Although it's up to you to decide what constitutes "meaningful" pain reduction, studies suggest that most individuals with chronic pain feel that an approximately 30 percent reduction in pain is meaningful to them.
- You should stop taking a medication if it causes you bad side effects, even if it seems to effectively reduce your pain.

## WHY SHOULD EVERY MEDICINE'S DOSE BE GRADUALLY INCREASED OR DECREASED?

In doctors' terms, the processes of increasing and decreasing a medication dose are known as *titration* and *tapering*, respectively. It is not known at which dose any medication for pain will work or cause side effects for any individual patient. As we mentioned earlier, every patient is different. Therefore, you will not be able to tell whether a medicine is the right one for you until it is titrated to the correct dose. Many people do not experience meaningful relief until they are taking the highest dose they can tolerate, meaning the largest dose they can comfortably take every day without experiencing bad side effects.

Also, very importantly, if you and your doctor agree that a certain medication for pain is not right for you and you both decide that you should be taken off the medication, you also need to decide how to stop it. Most often, it may be necessary to gradually reduce your dose. It may be dangerous and/or very unpleasant to stop taking certain medications such as opioids "cold turkey" because you may experience withdrawal symptoms (this does not mean you're "addicted!").

## WHAT ABOUT POTENTIAL LONG-TERM EFFECTS OF DRUGS?

This is a very important question. When your doctor prescribes medication for the treatment of chronic pain, he or she should tell you about the potential side effects after long-term use. Unlike treating acute pain, where a medication is prescribed for only a short period of time, if a medication is successful in treating your chronic pain it will be prescribed for an indefinite period of time—months or even years.

In addition to side effects that you may notice immediately, you must also be aware of potential adverse effects that may develop slowly and that you may not notice right away. Therefore, when prescribing a medication for chronic pain, your

doctor should explain to you any risks of taking that particular drug. Additionally, when taking a medication for a long period of time, it may be necessary for your doctor to screen you periodically for potential adverse effects associated with that drug, such as checking your liver or kidney function through blood tests as well as blood counts, depending on which drug you are taking.

## Rules For Taking Medications, Part II

If you are not following any of these rules right now, you should discuss these issues with your doctor so that you and your pain can be better treated.

### RULE 1: YOU HAVE TO GIVE THE MEDICATION A FAIR CHANCE TO WORK

Too often, people with chronic pain will stop taking a medication prematurely because they believe it doesn't work. What they don't realize is that if they had increased the dose gradually (under a doctor's supervision), they may have experienced excellent pain relief. You don't want to miss this potentially life-changing opportunity, do you?

### RULE 2: EACH MEDICATION SHOULD BE TAKEN DAILY ON A REGULAR SCHEDULE

Most medication for chronic pain should be prescribed around the clock to ensure that a steady level of the drug is in your system at all times. You should be taking the medicine every day at the same time(s)—not based on when your pain is bad—to keep the same amount of the drug in your body. (There are some exceptions to this rule for specific types of medicine, which we describe later in this chapter.)

### RULE 3: TRY TO MINIMIZE THE NUMBER OF DIFFERENT MEDICATIONS-FOR-PAIN THAT YOU ARE TAKING

You should always aim to take the least amount of medication possible. Remember what you just learned: You should continue taking a medication for pain only if it is giving you meaningful pain relief, with no or few side effects, and you are able to be more active. Many times, people stay on certain drugs seemingly forever, even when the drugs are not helping at all and should be stopped. All medication has potential side effects (and added costs!), so why take a drug if the benefit:risk ratio is not in your favor? You and your doctor should review every medication for pain you are taking at least every 3 months.

### Names of FDA-Approved Topical Pain Drugs (Brand Names)

- Lidocaine patch 5% (Lidoderm): FDA-approved for the relief of pain associated with postherpetic neuralgia (PHN)
- Topical diclofenac sodium topical solution 1.5% (Pennsaid): FDA-approved to treat the signs and symptoms of OA of the knee
- Diclofenac sodium topical gel 1% (Voltaren Gel): FDA-approved for relief of the pain of OA of joints amenable to topical treatment, such as the knees and hands
- Diclofenac epolamine topical patch (Flector): FDA-approved for the topical treatment of acute pain due to minor strains, sprains, and contusions

## Alert! Compounded Topical Drugs: Beware!

A compounding pharmacy is a type of pharmacy that will prepare a specialized medication to fill an individual patient prescription authorized by a doctor. Although compounding pharmacies are legal, they are not regulated by the FDA with respect to quality control. Compounding pharmacies use their own homegrown, poorly studied (and usually not studied at all!) concoctions that have not been evaluated by the FDA. The topical drugs that a compounding pharmacy may make for you have not been properly tested, and therefore:

- May not even penetrate the skin, and thus have no real effect on your pain
- May cause too much of the drug to penetrate the skin and get too much into the bloodstream, potentially causing serious side effects
- May cause severe skin reactions and allergies
- May interact negatively with its packaging and result in the absorption of potentially toxic compounds

## Commonly Used Medications For Pain

The NSAIDs are a first-line therapy for many chronic pain states, such as arthritis pain and certain types of headaches. However, in other states, such as chronic myofascial pain, neuropathic pain, and fibromyalgia, in which there is no significant degree of active inflammation, these drugs less commonly produce significant amounts of pain relief.

### NSAIDS

As the name implies, NSAIDs act by reducing the inflammatory response. Some recent studies have suggested that some of these drugs may produce pain relief by having a direct effect in the nervous system, independent of their anti-inflammatory activities.

### POTENTIAL ADVERSE EFFECTS ASSOCIATED WITH NSAIDS

Acute

- Nausea and stomach upset (except acetaminophen)

Long-term

- Liver abnormalities
- Kidney abnormalities
- Stomach or intestinal ulcers (does not generally apply to acetaminophen)
- Cardiovascular adverse events (heart attack, stroke, high blood pressure)
- New data is emerging that indicates chronic use can increase the risk of cardiovascular problems.
- If migraine patients take these drugs too often (daily or near daily), they may cause a daily headache syndrome called *rebound headache*.

### COX-2 INHIBITOR ANTI-INFLAMMATORY DRUGS

COX-2 inhibitors work on pain by decreasing the amount of inflammation at the site of injury, the same mechanism with which the traditional NSAIDs work. However, unlike the traditional NSAIDs, these drugs were designed in the laboratory to specifically interact with only the inflammation chemicals at the site of injury, and not to have any activity on similar chemicals that are also present elsewhere in the body, such as in the stomach. Thus, pharmaceutical companies designed these drugs in hopes of keeping the good and eliminating the bad effects of NSAIDs. Most of these drugs, like the NSAIDs, have also been shown to potentially increase the risk of cardiovascular adverse events.

These drugs have been shown to relieve pain associated with both rheumatoid arthritis (RA) and osteoarthritis (OA) pain, as well as treating acute pain from migraine headaches, tension-type headaches, and some musculoskeletal pain conditions, such as sprains and strains.

It is important to realize that COX-2 drugs have never been shown in studies to relieve pain better than NSAIDs. However, some pain sufferers do report that they feel COX-2 drugs give them better pain relief than NSAIDs.

### THE COX-2 LANDSCAPE AFTER VIOXX

Many of you may remember the media attention given to COX-2 inhibitors during their introduction and FDA hearings. In the late 1990s, we remember the full-blown cover stories in *Time* and *Newsweek* proclaiming them as "super aspirins" that would cure all pains without the side effects commonly associated with NSAIDs, such as gastritis and stomach ulcers, even when the studies showed that their pain relief wasn't any better than that provided by ibuprofen (Motrin and Advil).

In 1999, both Celebrex and Vioxx were introduced to the U.S. market and rapidly became the most frequently prescribed new drugs in the United States, with sales in the United States exceeding $3 billion in 2000 and more than 100 million prescriptions written that year. In 2001, Pfizer's sales of Celebrex alone amounted to $3.1 billion. Then suddenly, on September 27, 2004, Merck voluntarily took Vioxx (rofecoxib) off the market, due to studies suggesting an increased risk of heart attack and stroke.

In February 2005, the FDA Arthritis Drug Advisory Committee had several days of hearings on COX-2 inhibitors, evaluating studies of Celebrex, Bextra, and Vioxx. They concluded unanimously that all three of these drugs did increase the risk of heart attack and stroke, and recommended that the strongest possible warnings—so-called *Black-box Warnings*—be placed on the drugs' bottle or box to notify patients of these potential serious dangers. When the FDA asked the panel if each of the drugs should be banned, they voted 31 to 1 against banning Celebrex, 17 to 13 against banning Bextra, and 17 to 15 against banning Vioxx. The panelists of doctors and researchers believed that for some patients the benefits outweighed the risks, as long as both the prescribing doctor and the patient were made aware of the data.

In April 2005, Pfizer removed Bextra from the market. Today, in the United States only one COX-2 inhibitor is still on the market: Celebrex. Arcoxia, another Merck COX-2 inhibitor, is currently sold in Europe, Asia, and South America.

### Names of COX-2 Medications (Brand Names)

- Celecoxib (Celebrex)
- Rofecoxib (Vioxx):
  The manufacturer of Vioxx removed the drug from the market in 2005 because it caused an increased risk of cardiovascular adverse events (heart attack and stroke).
- Valdecoxib (Bextra):
  The FDA removed Bextra from the market in 2005 because it caused an increased risk of cardiovascular adverse events (heart attack and stroke).
- Etoricoxib (Arcoxia):
  This drug is not approved in the United States, but it is available in Europe, Asia, and Latin America.

## What's New: Lidocaine Patch 5% (Lidoderm)

Though other topical lidocaine formulations are available (and other topical novocaine-like drugs), Lidoderm is the only currently available local anesthetic drug formulation that causes pain relief (analgesia) without causing skin numbness (anesthesia). It is approved by the FDA to treat the chronic nerve pain of PHN. Clinical studies have also reported that it can also provide pain relief in other pain conditions, such as diabetic neuropathy pain, carpal tunnel syndrome, OA pain, and low back pain, although these uses are not FDA-approved.

Because its formulation is so unique, it should not be substituted for other topical lidocaine products. Many doctors and insurance companies do not understand this major difference, which has a significant effect on treatment efficacy.

**How does it work?** The lidocaine from the patch continually penetrates the skin and finds its way to the abnormal pain nerves under the skin that are causing electrical pain signals. When pain nerves get damaged or inflamed, they cause pain signals to go into the spinal cord and brain, even when there is no reason to. When lidocaine interacts with damaged or inflamed nerves, it quiets them down, resulting in fewer pain signals being sent to your brain.

## Topical Analgesics Reduce Side Effects

With the proper formulation (special ingredients to help the drug penetrate the skin), topical drugs can be excellent chronic pain medications for when the pain is coming from muscles, nerves, or joints. And because extremely little of the drug gets into the bloodstream, it is less common than with oral analgesics that serious side effects occur. As you would expect, the most likely side effects are skin reactions such as rashes, but these are not very common. Also, because little gets into the blood, there is very little chance of drug-to-drug interactions.

### HOW DOES A TOPICAL DRUG DIFFER FROM A TRANSDERMAL DRUG?

A lot of doctors and pharmacists still don't understand the critically important distinctions between topical and transdermal drug formulations. Like topical drugs, transdermal drugs are also applied to the skin, usually in a patch (Duragesic fentanyl pain patch, nicotine patch, estrogen patch, topical nitrates, etc.), though they can also be in a gel (testosterone gel). However, unlike topical drugs, transdermal drugs must result in the drug getting into the blood in significant amounts, since the drug doesn't work locally. For pain relief the drug must enter the brain, spinal cord, or organs to work. Therefore, the side effects of transdermal drugs are the same as those you can expect when taking the drug by mouth or injection since similar amounts of the medication enter the bloodstream.

## Topical NSAIDS Are First-Line Treatments

The recently FDA-approved topical NSAIDs are now first-line pain treatments for OA and sports injury pains (sprains, strains, and contusions). Although other topical NSAIDs have been available in other parts of the world, such as Europe, Asia, and Latin America, these formulations have little proven efficacy.

### TOPICAL NSAIDS (BRAND NAME)

- Topical diclofenac solution 1.5% (Pennsaid): FDA-approved for the signs and symptoms of OA of the knee
- Diclofenac topical gel 1% (Voltaren Gel): approved for the pain of OA of joints amenable to topical treatment, such as those of the knees and hands
- Diclofenac epolamine topical patch 1.3% (Flector Patch): approved for minor sports injury pain

### TOPICAL NSAID SIDE EFFECTS

- Acute: skin rash
- Chronic: minimal risk of gastrointestinal, renal, kidney, and cardiovascular problems
- The oral form has been associated rarely with liver abnormalities that most often self-resolve. This finding has also extremely rarely been reported in patients taking some topical diclofenac products; recently an FDA warning has been issued regarding the possibility of liver function abnormalities with use of Voltaren 1% gel. If you are prescribed the Voltaren 1% gel, be sure to ask your doctor to arrange for you to have blood tests done to check your liver function within 4 to 8 weeks of starting it. It may be that all drugs with the medication diclofenac present a risk for this adverse event.

## Antiseizure Medications (Neuromodulators)

For more than fifty years, drugs that have been used primarily to treat seizures (epilepsy) have also been used to treat certain types of chronic pain, such as neuropathic pain and migraines. In fact, since the mid–1990s, two of these seizure drugs (gabapentin and pregabalin) have become first-line treatments for many nerve pain (neuropathic pain) conditions. To lessen confusion among patients and doctors, some of these drugs are now also referred to as *neuromodulators.*

All of the antiseizure drugs are thought to reduce nerve pain by quieting the abnormal nerves that are signaling "pain" in the central nervous system, brain, and spinal cord. However, the way each antiseizure drug reduces these abnormal signals differs, since many of these drugs interact with different brain and spinal cord chemicals. It is still not known exactly how some of these medications work to alleviate pain.

### ANTISEIZURE MEDS HELP WITH NERVE PAIN

Antiseizure medications have been used to treat chronic nerve pain for several decades. It was originally thought that these drugs could help only with sharp, shooting, electric-like types of nerve pain. However, current research suggests that in many patients with nerve pain, these drugs can help with other types of pain qualities, including constant, dull, aching, or burning pain.

### What's New: Topical Diclofenac for OA: Pennsaid versus Voltaren Gel

It is important to recognize the different approved indicated uses of these drugs:

- Topical diclofenac sodium topical solution 1.5% (Pennsaid) is FDA-approved to treat the signs and symptoms of OA of the knee, meaning it has been proven to improve knee pain, physical function (your ability to do things), and overall well-being.
- Diclofenac sodium topical gel 1% (Voltaren Gel) is FDA-approved for the relief of pain of OA of the joints amenable to topical treatment, such as the knees and hands; it's been proven only to improve the pain associated with OA.
- Voltaren Gel failed to show an improvement of function and overall health in OA patients, whereas Pennsaid did prove that it relieves the pain of knee OA and improves function and overall health. Moreover, Pennsaid has demonstrated it relieves OA pain equally as well as an oral NSAID with fewer side effects, but Voltaren Gel has never been studied head-to-head with an oral NSAID.

(Disclaimer: Dr. Galer helped develop Pennsaid and his current employer helps market the drug.)

## Alert! Side Effects Associated with Antiseizure Medications

| Drug | Acute | Chronic |
|---|---|---|
| All | Dizziness<br>Sedation/fatigue<br>Memory/thinking difficulty | |
| Gabapentin (Neurontin) | Peripheral edema (swelling of feet, legs) | None currently known |
| Pregabalin (Lyrica) | Peripheral edema | None currently known |
| Topiramate (Topamax) | Tingling feelings<br>Loss of appetite | None currently known |
| Phenytoin (Dilantin) | Rare, possibly fatal, skin rash (Stevens-Johnson Syndrome) | Gingival hyperplasia (abnormal growth of gingiva in the mouth) |
| Carbamazepine (Tegretol) | Rare liver toxicity | Bone marrow suppression (rare)<br>Liver toxicity (rare)<br>–Note that blood needs to be checked regularly for blood count and liver function tests when taking carbamazepine |
| Valproic acid (Depakote) | Weight gain<br>Hair loss<br>Liver toxicity | Liver toxicity (blood needs to be checked regularly for liver function tests)<br>Weight gain |
| Lamotrigine (Lamictal) | Stevens-Johnson Syndrome | Stevens-Johnson Syndrome |
| Oxcarbazepine (Trileptal) | None currently known | None currently known |

The antiseizure drugs with the strongest evidence for efficacy in neuropathic pain conditions (e.g., PHN and painful diabetic peripheral neuropathy) are:

- Gabapentin (Neurontin): FDA-approved to treat PHN
- Pregabalin (Lyrica): FDA-approved to treat PHN and painful diabetic neuropathy
- Carbamazepine (Tegretol): FDA-approved to treat trigeminal neuralgia. Note that we haven't mentioned this drug in the Neuropathic Pain chapter because it should not be used for PHN, diabetic neuropathy, or RSD/CRPS. Because of its potential serious side effects, it should only be used first line to treat another uncommon nerve pain condition of the face called trigeminal neuralgia, where it works very reliably.

### CHRONIC MIGRAINES CAN BE RELIEVED

Growing scientific evidence also suggests that some antiseizure drugs, when taken daily, can help reduce the frequency of chronic migraines. The antiseizure drugs that have the strongest evidence for efficacy in treating chronic migraines are:

- Topiramate (Topamax): FDA-approved to prevent the occurrence of chronic migraines
- Valproic acid (Depakote): FDA-approved to prevent the occurrence of chronic migraines
- Gabapentin (Neurontin): not FDA-approved, but several studies have demonstrated efficacy

## Antidepressants Even If You're Not Blue

Antidepressants have been used to treat many different types of chronic pain for several decades. It is important to realize that these medications can be helpful in alleviating pain even if you are not depressed.

Two different types of antidepressant drugs are used to treat pain, and each works on different brain and spinal cord chemicals: tricyclic antidepressants (TCAs) and serotonergic noradrenergic reuptake inhibitors (SNRIs); see sidebar for examples of these medications. Another class of antidepressants, the serotonin-specific reuptake inhibitors (SSRIs), is sometimes used, but studies have not demonstrated that these drugs have major pain-relieving capabilities.

All of these drugs were first studied and used to treat depression, which is why they are still called *antidepressants*. When these drugs were initially discovered, doctors were unaware of their potential to help treat pain. In this section, we will outline the various types of antidepressant medications, as well as how they may be used to help treat your chronic pain.

### Types of Antiseizure Drugs (Brand Names)

Pregabalin (Lyrica)
Gabapentin (Neurontin)
Topiramate (Topamax)
Phenytoin (Dilantin)
Carbamazepine (Tegretol)
Oxcarbazepine (Trileptal)
Valproic acid (Depakote)
Lamotrigine (Lamictal)

### ACUTE SIDE EFFECTS ASSOCIATED WITH TCAS

- Anxiety/restlessness
- Confusion/poor memory
- Constipation
- Dizziness
- Drowsiness/fatigue
- Dry mouth
- Impaired vision
- Irregular heart rhythm*
- Nausea/loss of appetite/upset stomach
- Orthostatic hypotension (blood pressure falls with standing)*
- Sexual dysfunction
- Shaking
- Increased sweating
- Urinary retention
- Weight gain

* These side effects are rare, but they can lead to very serious consequences if they occur. Therefore, your doctor should check your blood pressure and EKG prior to prescribing a TCA drug and also while you are on this type of medication.

Though TCAs are commonly used to treat many chronic pain syndromes, a lot of patients—especially the elderly—cannot tolerate the side effects of these drugs. Thus, despite the potential benefit of these drugs, their side effects outweigh any pain-relieving effects they might provide. But, if other types of pain-relieving drugs are not working then the TCAs should still be tried.

### TCAS WORK

Doctors prescribe TCAs because they can be excellent pain relievers for people in many chronic pain states. Clinical studies have demonstrated that TCAs can relieve the pain of peripheral neuropathy (such as diabetic neuropathy), PHN, chronic low back pain, chronic migraine headaches, and chronic tension-type headaches.

It's important to note that these drugs often produce significant pain relief quicker and at much lower doses than are needed to treat depression. For instance, nortriptyline needs to be given at 150 mg per day for at least four weeks before it begins to relieve depression, whereas to treat migraines, tension-type headaches, or neuropathic pain the average dose is 10–50 mg per day, and its pain-relieving effect may occur within one week once the correct dose is found for a patient.

Chronic-pain patients and their doctors should also realize that different TCAs can affect the same person in distinct ways (both good and bad). Therefore, if you are not getting sufficient pain relief or if you are experiencing bad side effects from one TCA drug, that doesn't mean all TCAs will have the same effect on you. Because all the TCAs differ dramatically in how they affect the chemicals in your brain and spinal cord, you should try several TCA drugs before you give up on the possibility that these drugs might be of benefit to you.

### SSRIS DO NOT WORK WELL FOR PAIN

Unlike TCAs, most studies have shown that SSRIs do not relieve most pain conditions. In fact, except for their potential use in chronic migraine and chronic tension-type headache, these drugs are not considered good pain drugs as they have shown little to no pain-relieving abilities.

SSRIs are a class of medication widely prescribed to treat depression and anxiety. Thus, if you are depressed or you have an anxiety disorder (both of which are common in chronic pain patients due to their pain) these drugs may be a good choice for you, but to treat your psychological disorder, not to treat your pain.

### SEROTONERGIC AND NORADRENERGIC REUPTAKE INHIBITORS (SNRIS)

Clinical study evidence strongly suggests that the SNRI duloxetine (Cymbalta) can relieve several types of chronic pain, including neuropathic pain, fibromyalgia, OA pain, and chronic low back pain. In fact, duloxetine has FDA approval for use in treating diabetic peripheral neuropathic pain (DPNP) and fibromyalgia, and at the time of this writing it is under FDA review for a general chronic pain indication. Another SNRI, venlafaxine (Effexor), has some studies showing pain relief for the treatment of OA and some neuropathic pain. These drugs are also FDA-approved to treat depression and generalized anxiety disorder.

## Classes of Antidepressant Medications

**TCAs**

- Amitriptyline (Elavil)
- Nortriptyline (Pamelor)
- Desipramine (Norpramin)
- Doxepin (Sinequan)
- Imipramine (Tofranil)

**SNRIs**

- Venlafaxine (Effexor)
- Duloxetine (Cymbalta)
- Desvenlafaxine (Pristiq)

**SSRIs (not recommended to treat chronic pain)**

- Fluoxetine (Prozac)
- Paroxetine (Paxil)
- Sertraline (Zoloft)
- Citalopram (Celexa)
- Escitalopram (Lexapro)

## What's New: Duloxetine for the Management of Chronic Pain

Although the efficacy of duloxetine (Cymbalta) in managing diabetic painful neuropathy (DPN) has been established for some time, long-term data has been lacking. However, recent evidence suggests that the drug can alleviate the pain associated with DPN for more than six months. This is good news for patients with DPN who are looking for a "maintenance" medication.

**Can duloxetine be used to treat other types of pain?** Recently, convincing evidence shows that, in addition to treating DPN, duloxetine can improve pain and associated symptoms in patients with various arthritic conditions, chronic low back pain, and fibromyalgia. That is why the FDA is currently reviewing all the scientific study data to determine whether it should grant duloxetine a general "chronic pain" indication.

**Tizanidine (Zanaflex) for Tension-Type Headache**

Tizanidine is a fairly unique drug in that it acts on alpha-2-adrenergic receptors, a neurotransmitter system in the nerves and muscles, and is considered a "muscle relaxant" type of drug. However, like many pain-relieving medications, the specific mechanism by which this drug relieves pain is not known.

Studies have shown that tizanidine can reduce tension-type headaches in some patients. Other studies have shown that it also might work to alleviate pain in some people with acute back pain or musculoskeletal pain.

Based on these studies and clinical experience, we think tizanidine can be a good medication for the treatment of tension-type headaches and perhaps for patients with some muscle pains. However, many patients experience more side effects than pain relief from tizanidine. See Table 8.2.

**Table 8.2: Acute and Chronic Side Effects Associated with Tizanidine**

| | |
|---|---|
| **Acute** | • Sedation<br>• Dry mouth<br>• Decrease in blood pressure (uncommon) |
| **Chronic** | • Fatigue<br>• Increased liver enzymes (very uncommon) |

## Systemic Local Anesthetic Drugs

Systemic local anesthetic drugs, such as an intravenous lidocaine infusion and oral mexiletine, work in neuropathic pain therapy by quieting the abnormal pain signals being generated in injured nerves, in both the central nervous system (brain and spinal cord) as well as the peripheral nerves. Due to the potential serious side effects associated with these drugs, they are generally prescribed only by pain specialists.

### THE TWO TYPES OF SYSTEMIC LOCAL ANESTHETIC DRUGS (ROUTE OF ADMINISTRATION)

- Lidocaine (Intravenous Infusion): With intravenous lidocaine infusion, a doctor inserts an intravenous line into your arm and lidocaine slowly drips into your vein until a small amount is in your body, relieving your pain. Most commonly, this procedure takes place in a specialized pain clinic and may take several hours from start to finish.
- Mexiletine (pill): This oral tablet drug is FDA-approved to treat irregular heart rhythms, but it has been shown in some studies to relieve nerve pain for some patients.

Very good evidence suggests that an intravenous lidocaine infusion can significantly reduce many types of nerve injury pain, and also perhaps migraines. However, the problem with intravenous lidocaine infusions is that they provide most patients with only a few hours of pain relief. Rarely, though, some patients can experience days or even weeks of relief after one treatment. Studies have also shown that taking mexiletine (an oral pill) can also alleviate nerve pain, though many patients often experience intolerable side effects, most commonly nausea.

## Systemic versus Topical Lidocaine

Lidocaine is a drug that pain specialists use both as an intravenous injection and as a daily topical patch. Both ways of administering lidocaine have been shown to alleviate certain types of pains. However, injecting lidocaine into the bloodstream via an infusion ("systemic" administration) has a lot more potential side effects.

Systemic drugs work by entering the bloodstream and traveling throughout the body. Thus, all drugs taken orally (pills, capsules, tablets, etc.) are systemic drugs. All drugs given intravenously are systemic drugs. Many medications in a patch are also systemic (called *transdermal*), including fentanyl and hormones.

### Acute Side Effects Associated with SSRIs

- Anhedonia (inability to experience pleasure from normal activities)
- Anxiety/restlessness
- Diarrhea
- Dizziness
- Drowsiness/impaired sleep
- Headache or exacerbation of headache
- Nausea/loss of appetite/upset stomach
- Sexual dysfunction
- Shaking
- Urinary retention
- Weight gain

## Medication Alert!

**Acute Side Effects of Systemic Local Anesthetics**

Intravenous lidocaine infusion

- Dizziness
- Ringing in ears
- Irregular heart rhythm (this rarely occurs, because the treatment is given under a doctor's supervision and the drug is very slowly dripped into the bloodstream)

Mexiletine

- Nausea (this can be lessened by taking the drug with food)
- Diarrhea
- Dizziness
- Anxiety (in patients with a history of anxiety disorder)
- Irregular heart rhythm (this should rarely occur since the drug's dose should be very slowly increased and pain relief typically occurs at doses far below that which can affect the heart)

This differs from topical therapies that utilize the active medication formulated for topical delivery (e.g., Lidoderm [lidocaine patch 5%] and topical NSAIDs). These work locally in the skin, muscles, and peripheral nerves where the drug is applied. Very little amounts of the drug actually get into the bloodstream and thus overall are much safer than systemic drugs.

IV lidocaine infusion has mostly only been shown to work on neuropathic pain conditions, whereas the lidocaine patch has been shown to help patients with not only peripheral neuropathic pain but also OA, back pain, and other local pain conditions.

## Steroids Greatly Reduce Inflammation But Have Issues

Steroids are strong anti-inflammatory agents. Contrary to what some people believe, steroids are not pain relievers in the true sense; they have no direct mechanism for reducing pain. However, for a tiny percentage of chronic pain patients, steroids may be useful. When other drugs do not work, steroids can be given successfully in a pulsed oral dose (a high dose with a quick taper) for certain conditions, such as acute, difficult-to-treat migraines and during the early stages of Reflex Sympathetic Dystrophy (also known as *Complex Regional Pain Syndrome*). These drugs are also sometimes prescribed for certain types of chronic arthritis (including OA) and as interventional nerve block treatment for back pain.

### SIDE EFFECTS ASSOCIATED WITH STEROIDS

**Acute**

- Euphoria
- Gastrointestinal (e.g., nausea)
- Weight gain

**Chronic**

- Ulcer
- Osteoporosis
- Physical dependence (the steroid dose must be slowly decreased; if stopped suddenly, it could cause serious medical problems)
- Weight gain

## Sedative/Hypnotic Drugs Don't Kill Pain

As the name implies, these drugs cause you to feel sedated and have a "hypnotizing" effect. In other words, they make you feel tired and more relaxed, but they offer no true pain-relieving mechanism. In the past, sedative/hypnotic medications were sometimes used to treat chronic pain, despite a lack of evidence for their efficacy. Luckily, today these drugs are being prescribed less and less frequently for pain disorders. However, unfortunately, some doctors still prescribe sedatives/hypnotics, so it is important for you to learn about these medications and avoid them.

Although sedatives/hypnotics may make you feel less bothered by your pain, more often they cause people to fall asleep. Additionally, these drugs can cause cognitive impairment (e.g., memory and concentration deficits) and can lead to a number of chronic side effects, including a potential for both a physical dependence and an addiction. Briefly, physical dependence means that after taking a drug chronically for months, you may develop withdrawal symptoms if you stop the drug suddenly; addiction is when you lose control over taking the medication and you start to take the medication for reasons other than pain.

### TYPES OF SEDATIVE/HYPNOTIC DRUGS

The two major classes of sedatives/hypnotics are barbiturates and benzodiazepines. If any of the following drugs are prescribed to you to treat your chronic pain, you should ask your doctor for an alternative option.

**Barbiturates**

- Amobarbital (Amytal)
- Pentobarbital (Nembutal)
- Secobarbital (Seconal)
- Phenobarbitol (Luminal)

**Benzodiazepines**

- Alprazolam (Xanax)
- Chlordiazepoxide (Librium)
- Clonazepam (Klonopin)
- Diazepam (Valium)
- Estazolam (Prosom)
- Flunitrazepam (Rohypnol)
- Lorazepam (Ativan)
- Midazolam (Versed)
- Nitrazepam (Mogadon)
- Oxazepam (Serax)
- Temazepam (Restoril, Normison, Planum, Tenox, Temaze)
- Triazolam (Halcion)

### Sedative Alert!

**Chronic Side Effects of Sedatives/Hypnotics**

- Prolonged cognitive impairment
- Chronic fatigue
- Onset or worsening of depression
- Tolerance (needing increasingly larger doses to maintain the same effect)
- Physical dependence (if taken regularly, the patient will need to slowly taper off the medicine to avoid withdrawal syndrome)

Sedative/hypnotic medication does not produce pain relief in patients with chronic pain and may cause both acute and chronic side effects. **Sedative/hypnotic drugs are bad medications for management of chronic pain and should not be prescribed.**

### Alert! "Muscle Relaxants" Are Really Sedatives/Hypnotics

Note that we have put quotes around the term "muscle relaxants" because the drugs do not act directly on the muscle, but rather on the brain, much like the sedative/hypnotic drugs. They relax muscles by causing you to relax and feel tired. In fact, "muscle relaxants" are truly sedative/hypnotic drugs. Like those drugs, "muscle relaxant" medications do not produce pain relief in chronic pain states, and often cause both acute and chronic side effects. **"Muscle relaxants" are generally bad medications for chronic pain.**

#### MUSCLE RELAXANTS ARE OKAY FOR ACUTE PAIN

Muscle relaxants are sometimes used to treat acute pain conditions, such as muscle problems associated with acute back pain. However, for a number of reasons, including their relatively poor pain-relieving capabilities and their potential side effects, these drugs are not typically recommended for chronic pain.

#### TYPES OF MUSCLE RELAXANTS (BRAND NAME)

- Carisprodol (Soma)
- Baclofen (Lioresal)
- Cyclobenzaprine (Flexeril)
- Dantrolene (Dantrium)
- Metaxalone (Skelaxin)
- Methocarbamol (Robaxin)
- Orphenadrine (Norflex)

## Opioids' ("Narcotics") Historic Role

Opioid drugs are some of the oldest painkillers known to man. They have been used for thousands of years to treat all types of pain. Throughout time, and still today, no pain medication has had more controversy surrounding it than opioid drugs. It seems as though every decade there is a dramatic shift in medical wisdom as to what role these medications should play in the treatment of pain, especially chronic pain. In our medical careers, we have seen them play the role of both villain and superhero. In reality, they are more often the superhero than the villain, if prescribed appropriately to the right patient.

Besides being the drugs of choice for the treatment of acute moderate to severe pain from surgery or injury and for most types of cancer pain, opioid medication may also significantly relieve many patients' chronic pain. Over the past decade, lots of good scientific studies have shown that long-acting opioids can reduce the pain in some patients with low back pain, neuropathic pain, and arthritis pain.

Therefore, based on these studies and the experience of pain experts (like us), the vast majority of pain doctors feel that some patients with chronic pain can obtain significant pain relief from opioid medication, as long as they are prescribed and monitored properly (see "Who Is Appropriate for Opioid Medication?").

## NAMES OF OPIOID DRUGS

Opioids can be divided into two groups, based on how long their action lasts in the body: short-acting opioids and long-acting opioids.

### Short-Acting Opioid Drugs

- Tramadol (Ultram)
- Tramadol + acetaminophen (Ultracet)
- Codeine
- Oxycodone
- Oxycodone + acetaminophen (Percocet)
- Oxycodone + aspirin (Percodan)
- Hydrocodone + acetaminophen (Vicodin, Lortab)
- Morphine
- Meperedine (Demerol)
- Hydromorphone (Dilaudid)
- Oxymorphone IR (Opana IR)
- Transmucosal Fentanyl (Actiq, Fentora, Onsolis)
- Levorphanol

### Long-Acting Opioid Drugs

- Tramadol ER (Ultram ER, Ryzolt)
- Long-acting morphine (MS Contin, Morphine ER, Embeda Kadian, Avinza)
- Methadone
- Long-acting hydromorphone (Exalgo)
- Long-acting oxycodone (Oxycontin, Oxycodone ER)
- Oxymorphone ER (Opana ER)
- Transdermal fentanyl patch (Duragesic)
- Levorphanol

## OPIOID MEDICATION SIDE EFFECTS

### Acute side effects

- Gastrointestinal issues (nausea, vomiting)
- Constipation
- Itchiness
- Cognitive problems (memory, concentration

### Chronic side effects

Although all of the following have been associated with long-term opioid use, not every patient will experience these side effects, and some may lessen with time:

- Constipation
- Sedation
- Irritability
- Cognitive problems (memory and concentration problems)
- Hypogonadism (decreased libido, irregular menstrual cycle, impotence)
- Rebound headaches

## Help Stop Opioid Abuse

With the increased use of opioid medication to treat pain comes a societal cost. Specifically, some people take these drugs not to treat pain, but for their euphoric qualities. (Note that most pain patients do not experience euphoria from these drugs, but only find relief from the pain.) Taking opioid medication for euphoria can be very dangerous, if not fatal. When people overdose on these drugs—which is especially easy if they bite, chew, inject, or snort the long-acting opioids, such as Oxycontin, Opana ER, or Morphine ER—they can get a huge dose of the drug, causing them to stop breathing.

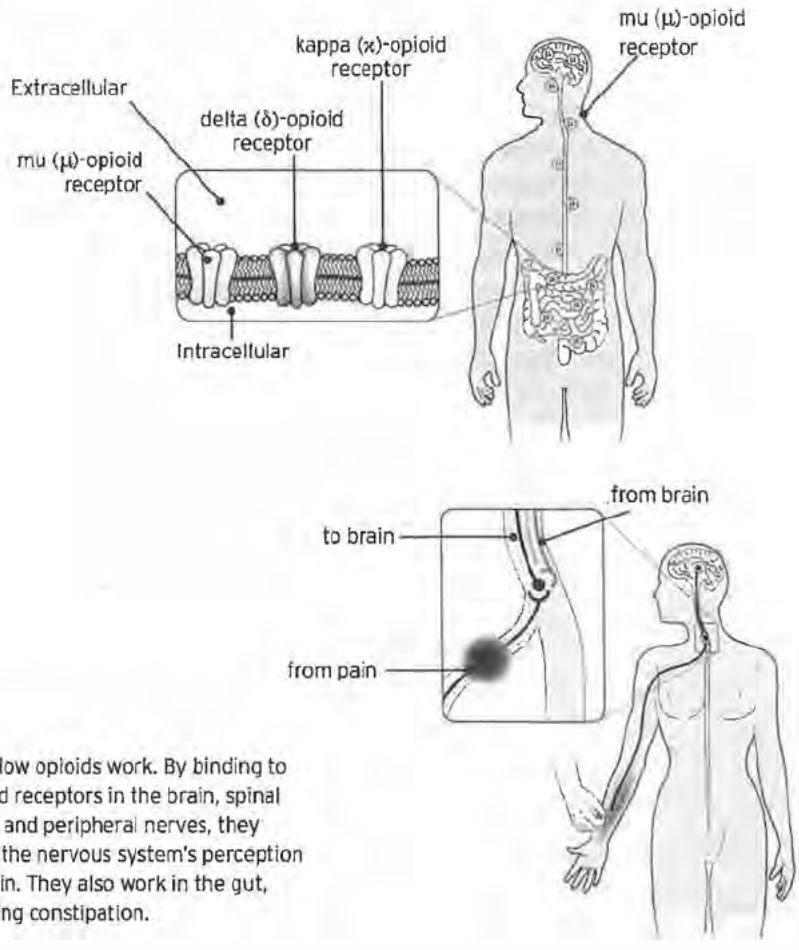
Studies have shown that the most common way nonpain persons get opioid pain medication is from a friend's or relative's medicine cabinet. Thus, one important way to stop the flow of opioid medication into society is to have a lock on your opioid medication and to dump it once you no longer need it. For the sake of the environment, please don't flush the pills down the toilet, but rather mix them with coffee grounds or cat litter and dispose of them in the garbage.

(continued)

### WHO IS APPROPRIATE FOR OPIOID MEDICATION?

It is currently recommended that every chronic pain patient suffering from moderate to severe pain be viewed as a potential candidate for opioid therapy. The only issue concerns when the patient should be prescribed an opioid. Like most pain treatment experts today, we believe chronic opioid therapy should not be a first-line treatment and should be tried only after other nonopioid medications have been tried and have failed.

As opposed to old medical myths, some chronic pain patients with back pain, neuropathic pain, and OA pain find that opioid drugs actually provide the best balance of pain relief and side effects. In fact, opioids in some ways are safer for elderly patients than many other pain drugs, such as TCAs and antiseizure drugs.




How opioids work. By binding to opioid receptors in the brain, spinal cord, and peripheral nerves, they alter the nervous system's perception of pain. They also work in the gut, causing constipation.

## Frequently Asked Questions About Opioids

### HOW DO OPIOIDS WORK?

All animals, humans included, have natural chemicals (neurotransmitters) called *endorphins* and *enkaphalins* in our brain and spinal cord, where they play a vital role in reducing pain. More recently, these natural chemicals have also been found in our peripheral nerves and joints, where it is thought that they also work to reduce pain.

Opioid medications act just like our natural opioid-like neurotransmitters. They work in the same places as do our body's natural opiate chemicals, the endorphins and enkaphalins, within our spinal cord, brain, peripheral nerves, and joints, to help alleviate pain.

### WHERE DO OPIOID DRUGS COME FROM?

There are several different types of opioid drugs:

- Natural opiates come from opium poppy resin and include morphine and codeine.
- Semisynthetic opioids are made using natural opiates and include hydromorphone, hydrocodone, oxycodone, and oxymorphone.
- Fully synthetic (man-made) opioids include fentanyl, methadone, and tramadol.
- Endogenous opioid chemicals are produced naturally in the body and include endorphins, enkephalins, dynorphins, and endomorphins.

### DO OPIOIDS CAUSE ADDICTION IN CHRONIC PAIN PATIENTS?

First, we need to define what addiction is and is not. So many people confuse addiction with another biologic process, physical dependence. We're sure you have read the newspapers and seen on TV the accounts of people claiming to have become addicted to Oxycontin. Absolutely this is a major societal issue that needs to be dealt with. However, in our opinion, many of these folks on TV appeared not to be addicted, but rather had developed a physical dependence, which is a normal bodily reaction that happens with lots of different types of medication, including medications not used for pain, and is easily remedied.

(Help Stop Opioid Abuse continued)

**FDA Steps In** Because of all the issues with the abuse of opioid medication, the FDA has very appropriately instituted measures drug companies need to take while they are marketing these medications. The FDA has now required makers of opioid medications to institute risk-evaluation and mitigation strategies (REMS) to address the issues of abuse and misuse of these medications. Also, at the time of this writing, the FDA is contemplating a required learning course for all doctors who prescribe opioid medications and patients who take them, which we believe is a good idea.

## What's New: Opioids that May Deter Abuse

Due to the societal issue of misuse of opioid drugs, drug companies have developed special formulations of their extended-release opioids that may make misuse less likely, and if abused, may less likely result in death.

**How do these work?** One drug recently approved by the FDA, Embeda, combines extended-release morphine with the anti-opioid naltrexone. Embeda results in the same amount of pain relief as morphine, but if the capsule is tampered with, naltrexone is released and works against the morphine, preventing death from respiratory depression.

Multiple other abuse-deterrent opioids are being developed with various other technologies, including pills that cannot be crushed.

Physical dependence is a natural occurrence that happens to everyone who takes certain drugs for a long period of time. Your body gets used to having the drug, so when you stop taking it, you will develop a negative withdrawal reaction. This happens not just with opioids, but also with nicotine, caffeine, alcohol, sedatives/hypnotics (e.g., Valium), antidepressants, blood pressure drugs, and steroids. Going into withdrawal after suddenly stopping an opioid does not mean you are addicted. Opioids, even if taken chronically, can be safely and comfortably stopped by gradually reducing the dosage, usually by 10 percent every five to seven days.

By definition, addiction is a psychological craving for a drug, and is apparent when a person takes an opioid for reasons other than pain relief. The addict lives every minute of the day thinking about how he or she will get his or her next dose of that drug. When chronic pain patients take opioids to treat their pain, they rarely develop a true addiction and drug craving. However, a risk factor for developing a true addiction to opioid medications, even if you are taking them for pain, is a history of a prior addiction, such as to alcohol or other drugs.

### Pseudoaddiction Because of a Low Dose

Sometimes chronic pain patients may develop something called *pseudoaddiction*, which is caused by their doctor not appropriately prescribing the opioid medication. Pseudoaddiction happens when a patient's opioid medication is not being prescribed in doses strong enough to provide good pain relief, or the drug is not being prescribed often enough throughout the day. If this is the case, because the pain patient is still experiencing pain, he or she begins to take more doses than were prescribed to achieve good pain relief (and not for the high). Although this is a serious no-no, it is not a true addiction because the patient is not taking extra doses of the opioid medication to maintain a high, but rather is taking the extra pills to relieve pain. When a pseudoaddicted patient is prescribed the proper amount of opioid medication, he or she doesn't take any extra pills, because his or her pain is relieved.

### Tolerance Is a Natural Reaction

Some pain patients (and even some of their doctors) mistakenly feel they are addicted because over time they need to take increasingly larger doses of the same opioid medication to experience the same amount of pain relief. This is called

*tolerance*. Tolerance is a natural physical reaction and is not addiction. To be tolerant to opioids, a patient must first have demonstrated significant pain relief at a certain dose which remains stable for at least a month.

Also, in our experience, the issue of tolerance is overblown. Only a minority of chronic pain patients who are taking long-term opioids develop tolerance.

### Physical Dependence

Physical dependence is not addiction! Lots of other non-narcotic drugs also produce a physical dependence, such as steroids, blood pressure medicine, and antidepressants. Physical dependence is another naturally occurring physical reaction that happens in everyone! All patients can safely be taken off opioid medication if the dose is slowly tapered down by their doctor.

**The bottom line:** Only rarely does opioid medication cause a true addiction when prescribed appropriately to a chronic pain patient who does not have a prior history of addiction.

## HOW SHOULD OPIOID MEDICATION BE PRESCRIBED?

When using an opioid as one of the main treatments for chronic pain, long-acting opioid formulations are better than short-acting ones. Long-acting opioid medications should be prescribed around the clock, meaning that you take them at certain times on the clock (usually twice per day or once per day) and not based on how much pain you are feeling. This around-the-clock dosing results in a steady, constant amount of the drug in your blood, and therefore keeps you consistently more comfortable throughout the full twenty-four-hour cycle.

## CONCLUSION: FIND THE DRUG THAT WORKS FOR YOU

As you have seen, you have an almost overwhelming number of medication options to consider when working with a doctor to treat your chronic pain. The appropriate choice will depend on your specific condition, the severity of the drug's side effects, and simply, what works best for you. In finding the ideal drug or drugs, it is important to remember to be patient and persistent. If the first one does not succeed, try and try again. It is critical for you to find a doctor who is familiar with how to prescribe all of these medications, and one who, like you, won't give up trying!

## Q & A *with Dr. Argoff and Dr. Galer*

**I have nerve pain in my feet from diabetes. The doctor says there's not much to try except Percocet or Vicodin. Is this true?**

No. While opioid narcotic medication, such as the oxycodone in Percocet and the hydrocodone in Vicodin, can alleviate all types of nerve pains, they are not the only medications that can treat neuropathic (nerve) pain and also likely shouldn't be the first medication to try most of the time. Nerve pains, whether from diabetes, shingles, or other types of nerve injury, can be successfully treated with many different types of drugs. While the FDA has approved only several medications to treat pain from diabetic neuropathy, including Pregabalin (Lyrica) and Duolexetine (Cymbalta), other drugs have been approved by FDA to treat Postherpetic Neuralgia, such as Lidocaine Patch (Lidoderm) and Gabapentin (Neurontin). Most pain experts agree that if a drug has been shown to treat one type of nerve pain problem it most likely can also help alleviate other kinds of nerve injury pains.

**My doctor has kept me on the same medications to treat my pain for three years. I am not sure if they're helping me anymore. What should I do?**

First, remember all medication changes must be reviewed with your doctor and she or he has to agree to such changes and monitor every change.

This is a very good question that many patients have or should be asking themselves. Any medications you take (whether for pain or any other condition) should only be taken if it is helping and not hurting you. For pain, that usually means that it is providing at least 30% pain relief and has no bad side effects. However, sometimes patients after a while aren't sure if the medication is working. The best way to tell is to see what happens as you slowly decrease the dose–does the pain get worse? Again, this must be done under your doctor's supervision. The good news is that if your current treatment is not helping you as much as in the past, it is likely that your doctor can consider a newer regimen that may be more helpful.

**I am a 35-year-old with chronic back pain. Nothing has seemed to work, even two surgeries, nerve blocks, physical therapy, accupuncture and an electrical stimulator. I take Vicodin every once in a while and it really helps without any bad side effects. My doctor wants to put me on a strong opioid narcotic that I take every day, twice per day. I am afraid I'll become addicted, but the pain is just getting intolerable. What should I do?**

Here are the facts. It is very uncommon for a person with chronic pain to become "addicted" to narcotics IF (1) he doesn't have a prior history of any addiction and (2) he only takes the medication to treat pain. Studies have shown that many chronic pain patients can experience significant pain relief with tolerable side effects from opioid narcotic medication when taken daily and no addiction. We definitely would try this type of treatment for our patients in your situation.